Remarks

The Office Action issued November 29, 2007 has been received and reviewed. Claims 9-22, 25-34, and 56 are canceled without prejudice. Claim 1 is amended. Claims 57-61 are added. After entry of the amendment, claims 1-3 and 57-61 will be pending and under consideration. Reconsideration and withdrawal of the rejections are respectfully requested.

Claim Amendments

Claims 9-22, 25-34, and 56 are canceled without prejudice.

Claim 1 is amended to recite that the extent of difference in modulation is at least a two-fold difference. Support for the amendment may be found in Applicants' specification at, for example, from page 10, line 25 through page 11, line 8.

Claim 1 is also amended to recite that the TLR-mediated cellular response is includes the known responses of inducing production of a cytokine, co-stimulatory marker, intercellular adhesion molecule, proliferation/maturation marker, or a combination thereof. Support for the amendment may be found in Applicants' specification at, for example, page 10, lines 3-10.

New claims 57-60 recite particular TLR-mediated cellular activities. Support for claims 57-60 may be found in Applicants' disclosure at, for example, page 10, lines 3-10.

New claim 61 specifies particular human cell populations that naturally express TLR7 or TLR8. Support for the amendment may be found in Applicants' disclosure at, for example, page 22, lines 20-30.

The 35 U.S.C. §112, Second Paragraph, Rejection

Claims 1-3, 9-22, and 25-34, and 56 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Applicants respectfully traverse.

Claim 1 is independent. Claims 9-22, 25-24, and 56 are canceled. Each of claims 2 and 3 depends from claim 1. Thus, remarks that refer to claim 1 apply equally to claims 2 and 3.

The Office Action asserts that claim 1 is said to be indefinite because the not all of the cellular activities mediated by TLR7 and TLR8 are disclosed and they are not all known in the art. The amendments to claim 1 obviate the rejection by reciting "cellular activity known to be TLR7-mediated" and "cellular activity known to be TLR8-mediated."

The Office Action further asserts that claim 1 is indefinite because it lacks positive steps and proper controls. Applicants respectfully disagree.

Claim 1 recites a method of identifying a compound that selectively modulates at least one TLR-mediated cellular activity. The claimed method includes all positive steps necessary to practice the method: providing appropriate assays, performing the assays, and identifying the test compound as selectively modulating at least one of the assayed TLR-mediated cellular activities if the results of the assays meet specified criteria.

Moreover, Applicants' disclosure addresses this issue of controls at, for example, page 8, lines 15-22. Modulation of cellular activity refers to modulation in reference to an appropriate control. Furthermore, "[w]ith experience, one skilled in the art may develop sufficient familiarity with a particular assay (e.g., the range of values observed in an appropriate control under specific assay conditions) that performing a control may not always be necessary to determine whether a compound modulates the TLR-mediated cellular activity in a particular assay."

Therefore, Applicants respectfully submit that claims 1-3 satisfy 35 U.S.C. §112, second paragraph, and request that the rejection be withdrawn.

The 35 U.S.C. §112, First Paragraph, Rejection (Enablement)

Claims 1-3, 25-34, and 56 stand rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 1 is independent. Claims 9-22, 25-24, and 56 are canceled. Each of claims 2 and 3 depends from claim 1. Thus, remarks that refer to claim 1 apply equally to claims 2 and 3.

The basis for the rejection of claims 1-3 as not being enabled by Applicants' specification is unclear. The remarks in the Office Action appear directed to the method of claim 25, which is canceled herein. Thus, Applicants respectfully request that if claims 1-3, as amended herein, are considered to fail to satisfy the enablement requirement of 35 U.S.C. §112, first paragraph, that the next Office Action be made non-final in order to provide Applicants with a full and fair opportunity to address the enablement of claims 1-3.

For example, the Office Action states that the instant specification does not enable 'all possible' human cells that naturally express TLR7 or TLR8, acknowledges that Applicants' specification discloses human cell populations that naturally express either TLR7 or TLR8, but asserts that this disclosure fails to enable the genus of all possible human cells that express TLR7 and/or TLR8 (Office Action, page 7). The Office Action further cites *Genentech, Inc. v. Novo Nordisk A/S* for the rule that the specification, not the knowledge of one skilled in the art must supply the novel aspects of the invention.

Applicants submit that the teaching of the specification—i.e., the use of certain cell populations to screen for compounds that selectively modulate TLR-mediated cellular activity—enables one skilled in the art to practice the claimed method using <u>any</u> cell known to naturally express TLR7 or TLR8. The identity of the particular TLR7- or TLR8-expressing cell used in the assay is not critical to practicing the method. Moreover, contrary to the apparent assertion in the Office Action, the specific cell populations employed in the assays are <u>not</u> the novel aspects of the invention—Applicants are not claiming novel TLR7-expressing or TLR8-expressing cells. Claim 1 is directed to a screening method that employs already known cell populations in a new and useful manner to (a) obtain novel information about certain compounds, and (b) identify compounds that have TLR-related activities that meet the criteria recited in the claim. Finally, the Office Action provides no reason why the disclosure of the cited method using pDCs and mDCs fails to enable one skilled in the art to practice the claimed method using any <u>other</u> cell that one skilled in the art would recognize as naturally expressing TLR7 or TLR8.

Moreover, the amendments to claim 1 recite "cellular activity known to be TLR7-mediated" and "cellular activity known to be TLR8-mediated," the detection of which are fully enabled by Applicants' disclosure.

Applicants respectfully submit that claims 1-3 meet the enablement requirement of 35 U.S.C. §112, first paragraph, and request that the rejection be withdrawn.

The 35 U.S.C. §103 Rejection

Claims 1-3, 25-33, and 56 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Hornung *et al.* (*J. Immunol.*, vol. 168, 4531-4537 (2002), hereinafter, "Hornung") in view of Gibson *et al.* (*Cell. Immunol.*, vol. 218, 74-86 (2002), hereinafter, "Gibson"). Applicants respectfully traverse.

Claim 1 is independent. Claims 25-33, and 56 are canceled. Each of claims 2 and 3 depends from claim 1. Thus, remarks that refer to claim 1 apply equally to claims 2 and 3.

M.P.E.P. §706.02(j) states, "To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

Applicants respectfully submit that claim 1 is patentable over the combination of Hornung and Gibson because, at a minimum, the combination of Hornung and Gibson fails to teach or suggest all of the features recited claim 1. Applicants further submit that the combination fails to provide motivation to modify Hornung in a way that would result in the method of claim 1. Finally, Applicants submit that the combination of Hornung and Gibson fails to provide one skilled in the art with a reasonable expectation of successfully practicing the method recited in claim 1.

M.P.E.P. §2141.02 states, "In determining the differences between the prior art and the claims, the question under 35 U.S.C. 103 is not whether the differences themselves would have been obvious, but whether the claimed invention as a whole would have been obvious." (citations omitted, emphasis in original).

Applicants submit that the combination of Hornung and Gibson fail to teach or suggest a single method in which TLR7-mediated cellular activity is assayed and TLR8-mediated cellular activity is assayed. Also, the combination of Hornung and Gibson fails to teach or suggest comparing the results of the TLR7 assay and the TLR8 assay in order to determine whether a test compound modulates one TLR-mediated cellular activity to an extent that is at least two-fold greater than the extent to which the compound modulates the other TLR-mediated cellular activity.

The Office Action acknowledges that Hornung fails to "teach a method of identifying compounds that modulate TLR7 or TLR8." (Office Action, page 9). The Office Actionasserts that Gibson cures this deficiency in Hornung because Gibson is asserted to teach "that TLR7 agonists stimulate plasmacytoid dendritic cells (pDC) to produce a number of cytokines..." and "...a method of screening for compounds that modulate a TLR-mediated cellular activity (e.g. TNF-α, IP-10), and provide a means of testing this effect." *Id.*

The Office Action fails to identify any portion of Gibson that cures the deficiencies of Hornung with respect to teaching or suggesting the subject matter, as a whole, that is recited in claim 1. Gibson teaches only methods of screening for compounds that modulate TLR7 and, therefore, fails to cure the deficiency—acknowledged in the Office Action—of Hornung related to screening compounds that modulate TLR8. Moreover, neither Gibson nor Hornung teaches or suggests screening a single compound to determine whether it modulates both TLR7-mediated cellular activity and TLR8-mediated cellular activity, and then identifying the compound as selectively modulating a TLR-mediated cellular activity if the compound modulates the TLR7-mediated activity to different extent (i.e., at least two-fold) than it modulates the TLR8-mediated cellular activity. Thus, the combination of Hornung and Gibson fails to teach or suggest all of

the features recited in claim 1, as a whole. For at least this reason, the combination of Hornung and Gibson fails to establish a *prima facie* case of obviousness against claims 1-3.

Similarly, the combination of Hornung and Gibson fails to motivate one skilled in the art to modify the teachings of Hornung to practice the method recited in claim 1. Nothing in Hornung or Gibson would have motivated one skilled in the art to modify Hornung in order to arrive at a method in which a single compound is tested for its ability to modulate TLR7-mediated cellular activity and TLR8-mediated cellular activity, and then consider whether the compound modulates one activity to a greater extent than it modulates the other activity. Thus, the combination of Hornung and Gibson fails to motivate one skilled in the art to modify the teachings of Hornung to practice the method recited in claim 1. For at least this reason, the combination of Hornung and Gibson fails to establish a *prima facie* case of obviousness against claims 1-3.

Finally, the combination of Hornung and Gibson fails to provide one skilled in the art with a reasonable expectation of success practicing the method recited in claim 1. Specifically, the combination fails to provide one skilled in the art with a reasonable expectation of screening compounds for the ability to modulate a TLR8-mediated cellular activity. More importantly, the combination fails to provide one skilled in the art with a reasonable expectation of identifying a compound that modulates a TLR7-mediated cellular activity to an extent that differs from the extent to which the compound modulates a TLR8-mediated cellular activity. Thus, the combination of Hornung and Gibson fails to provide one skilled in the art with a reasonable expectation of practicing the method, as a whole, recited in claim 1. For at least this reason, the combination of Hornung and Gibson fails to establish a *prima facie* case of obviousness against claims 1-3.

Applicants respectfully submit that the combination of Hornung and Gibson fails to teach or suggest all of the features recited in claim 1, fails to motivate one skilled in the art to modify Hornung as necessary to practice the method recited in claim 1, and fails to provide one skilled in the art with a reasonable expectation of successfully practicing the method recited in claim 1.

Accordingly, Applicants respectfully submit that the combination of Hornung and Gibson fails to establish a *prima facie* case of obviousness against the subject matter, as a whole, recited in claim 1.

Applicants therefore respectfully submit that claims 1-3 comply with 35 U.S.C. §103(a) and request that the rejection of claims 1-3 as being unpatentable over Hornung in view of Gibson be withdrawn.

Summary

It is respectfully submitted that the pending claims 1-3 and 57-61 are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted
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CERTIFICATE UNDER 37 CFR §1.8:
The undersigned hereby certifies that the paper(s), as described hereinabove, are being transmitted via the U.S. Patent and Trademark Office electronic filing system in accordance with 37 CFR §1.6(a)(4) to the Patent and Trademark Office addressed to the Commissioner for Patents, Mail Stop **Amendment**, P.O. Box 1450, Alexandria, VA 22313-1450, on this 29th day of May, 2008.

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